Attorney Docket No.: 03678.0064.00US00

THE AMENDMENTS

In the Claims

1. (Currently Amended) A pharmaceutical formulation comprising a compound of general formula I, or salts thereof <u>and a pharmaceutically acceptable carrier</u>:

Formula I

wherein:

 X_1 , X_2 , and X_3 are independently selected from the group consisting of oxygen, methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido; T, W, and V are independently oxygen or sulfur;

m=0, 1 or 2;

n=0, 1, or 2;

p=0, 1, or 2;

M= H or a pharmaceutically-acceptable inorganic or organic counterion;

 $D_1 = O \text{ or } C$;

B' is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the 1' position of the furanose or carbocycle via the 9- or 1- position, respectively;

A is M or alkyl; or

A is a nucleoside residue which is defined as:

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$$B_{\nu_{\nu_{1}}}$$
 D_{2}
 Z

and which is linked to the phosphate chain via the 5' position of the furanose or carbocycle; wherein:

 $D_2 = O \text{ or } C$;

B is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the sugar or carbocycle via the 9- or 1- position, respectively;

wherein when D_1 and D_2 are oxygen, the furanose is in the β -configuration;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general Formula II or III;

Z'= OH or OR₂, where OR₂ falls under the definition of general Formula II or III;

Z= OH or OR₃, where OR₃ falls under the definition of general Formula II or III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general Formula II or III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively;

wherein compounds of general Formula I are molecules whose structures fall within the definitions of Formula Ia and Formula Ib:

Formula Ia

wherein:

$$\begin{bmatrix} H & H & O & \begin{bmatrix} T & & W & V & T & & B' \\ P & X_3 & P & X_2 & P & X_1 & P & O & & D_1 \\ OM & OM & OM & OM & OM & OM & OM \\ \end{bmatrix}$$

 $X_1, X_2, \text{ and } X_3=0;$

T, V, and W = O;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR_1 , where OR_1 falls under the definition of general formula II;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula Π ;

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Z= OH or OR_3, where OR_3 falls under the definition of general formula II;
Y= H, OH, or OR<sub>4</sub>, where OR<sub>4</sub> falls under the definition of general formula II;
provided that at least one of Y', Z', Z, and Y is OR<sub>1</sub>, OR<sub>2</sub>, OR<sub>3</sub>, or OR<sub>4</sub>, respectively;
D_1 = 0;
D_2 = O \text{ or } C;
B and B' are purine or pyrimidine residues according to general formulas IV and V;
m and p = 0, 1 \text{ or } 2;
n=0 or 1;
such that the sum of m+n+p is from 0 to 5; or
X_1, X_2, \text{ and } X_3=0;
T, V, and W = O;
M=H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> or other pharmaceutically-acceptable inorganic or organic counterion;
counterion;
Y'=H, OH, or OR<sub>1</sub>, where OR<sub>1</sub> falls under the definition of general formula III;
Z'=OH or OR_2, where OR_2 falls under the definition of general formula III;
Z= OH or OR<sub>3</sub>, where OR<sub>3</sub> falls under the definition of general formula III;
Y= H, OH, or OR_4, where OR_4 falls under the definition of general formula III;
provided that at least one of Y', Z', Z, and Y is OR<sub>1</sub>, OR<sub>2</sub>, OR<sub>3</sub>, or OR<sub>4</sub>, respectively;
D_1 = 0;
D_2 = O \text{ or } C;
B and B' are purine or pyrimidine residues according to general formulas IV and V;
m and p = 0, 1 \text{ or } 2;
n = 0 \text{ or } 1;
such that the sum of m+n+p is from 0 to 5; or
X_1 and X_3=0;
X<sub>2</sub> is selected from the group consisting of methylene, monochloromethylene,
dichloromethylene, monofluoromethylene, difluoromethylene, and imido;
T, V, and W = O;
M= H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> or other pharmaceutically-acceptable inorganic or organic counterion;
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counterion;

 X_1 and $X_3=0$;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula II; Z'=OH or OR_2 , where OR_2 falls under the definition of general formula II; Z=OH or OR_3 , where OR_3 falls under the definition of general formula II; Y = H, OH, or OR₄, where OR₄ falls under the definition of general formula II; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively; $D_1 = 0;$ $D_2 = O \text{ or } C$; B and B' are purine or pyrimidine residues according to general formulas IV and V; m and p = 0, 1 or 2;n=1; such that the sum of m+n+p is from [0] 1 to 5; or X_1 and $X_3=0$; X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido; T, V, and W = O; M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion; Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III; Z'=OH or OR_2 , where OR_2 falls under the definition of general formula III; Z=OH or OR₃, where OR₃ falls under the definition of general formula III; Y= H, OH, or OR_4 , where OR_4 falls under the definition of general formula III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively; $D_1 = 0$; D₂ is O or C; B and B' are purine or pyrimidine residues according to general formulas IV and V; m and p=0, 1 or 2;n=1; such that the sum of m+n+p is from [[0]] 1 to 5; or

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X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T=S;

V and W=O;

M=H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula II;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula II;

Z= OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively;

 $D_1 = 0;$

 $D_2 = O \text{ or } C$;

B and B' are purine or pyrimidine residues according to general formulas IV and V; m, n, and p=1; or

 X_1 and $X_3=0$;

 X_2 is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T=S;

V and W=O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula III;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III; provided that at least one of Y', Z', Z, and Y is OR1, OR2, OR3, or OR4 OR₁, OR₂, OR₃, or OR₄, respectively;

 $D_1 = 0;$

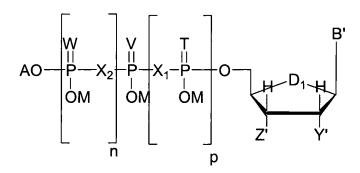
 $D_2 = O \text{ or } C$;

B and B' are purine or pyrimidine residues according to general formulas IV and V;

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m, n, and p=1;

Formula Ib



wherein:

A is M or alkyl;

 X_1 and $X_2 = O$;

T, V, and W = O;

M=H, NH₄⁺, Na or other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= H, OH or OR₂, where OR₂ falls under the definition of general formula II;

with the provision that at least one of Y' and Z' is OR₁ or OR₂;

$$D_1 = O \text{ or } C$$
;

B' is purine or pyrimidine residue according to general formulas IV and V; n and p are 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or

A is M or alkyl;

 X_1 and $X_2 = O$;

T, V, and W = O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

 $Y' = OR_1$, where OR_1 falls under the definition of general formula III;

 $Z' = OR_2$, where OR_2 falls under the definition of general formula III;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V;

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n and p are 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or

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A is M or alkyl;
X_1 and X_2 = O;
T and V = O;
W=S;
M= H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> or other pharmaceutically-acceptable inorganic or organic counterion;
Y'= H, OH, or OR_1, where OR_1 falls under the definition of general formula II;
Z'=H, OH or OR_2, where OR_2 falls under the definition of general formula II;
with the provision that at least one of Y' and Z' is OR<sub>1</sub> or OR<sub>2</sub>;
D_1 = O \text{ or } C;
B' is purine or pyrimidine residue according to general formulas IV and V;
p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;
n=1; or
A is M or alkyl;
X_1 and X_2 = 0;
T and V = O;
W=S;
M is selected from the group consisting of H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> and other pharmaceutically-acceptable
inorganic or organic counterion;
Y'=OR_1, where OR_1 falls under the definition of general formula III;
Z' = OR_2, where OR_2 falls under the definition of general formula III;
D_1 = O \text{ or } C;
B' is purine or pyrimidine residue according to general formulas IV and V;
p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;
n=1; or
A is M or alkyl;
X_1 = 0;
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X₂ is selected from the group consisting of methylene, monochloromethylene,

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dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M is selected from the group consisting of H, NH₄, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'=H, OH_2 or OR_2 , where OR_2 falls under the definition of general formula II;

with the provision that at least one of Y' and Z' is OR₁ or OR₂;

 $D_1 = O \text{ or } C;$

B' is purine or pyrimidine residue according to general formulas IV and V;

p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;

n=1; or

A is M or alkyl;

 $X_1 = 0;$

X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'= H, OH₂ or OR₂, where OR₂ falls under the definition of general formula III;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V;

p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;

n=1;

wherein, for compounds according to Formula Ia or Ib, where $Y' = OR_1$, $Z' = OR_2$, $Z = OR_3$ and/or $Y = OR_4$, at least one of the four is a residue which is linked directly to the corresponding 2' or 3' hydroxyl oxygen of the furanose or carbocycle via a carbon atom; wherein said residue falls within the scope of formula II or formula III:

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Formula II

$$-0$$
 Q R_5 R_7

wherein:

O is the corresponding 2' or 3' oxygen of the furanose or carbocycle;

R₅, R₆, and R₇ are selected from the group consisting of H, an alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety defined according to formula II is an ether; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q, and R₇ is selected from the group consisting of alkyl, cycloalkyl, aralkyl, and substituted aralkyl, such that the moiety defined according to formula II is an ester or thioester; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q, and R₇ is amino or mono- or disubstituted amino, where the substituents are selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety according to formula II is a carbamate or thiocarbamate; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q, and R₇ is selected from the group consisting of alkoxy, cycloalkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula II is a carbonate or thiocarbonate; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q and both the 2' and 3' oxygens of the furanose are directly bound to Q to form a cyclical carbonate or thiocarbonate, R₇ is not present;

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Formula III

wherein:

O is the 2' and 3' oxygens of the furanose or carbocycle; and

the 2' and 3' oxygens of the furanose or carbocycle are linked by a common carbon atom to form a cyclical acetal, cyclical ketal, or cyclical orthoester; and

for cyclical acetals and ketals, R₈ and R₉ are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl; or are joined together to form a homocyclic or heterocyclic ring composed of 3 to 8 atoms, or for cyclical orthoesters, R₈ is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl,

and R₉ is selected from the group consisting of alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy;

B and B' are independently a purine residue, as in formula IV, linked through the 9- position, or a pyrimidine residue, as in formula V, linked through the 1- position;

wherein, provided when D₁ and D₂ are oxygen, the ribosyl moieties are in the D- configuration;

Formula IV

$$R_{12}$$
 J_{8}
 J_{9}
 J_{13}
 J_{13}
 J_{12}
 J_{12}
 J_{13}
 J_{13}

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Formula V

$$R_{16}$$
 A_{16}
 A_{15}
 A_{15}
 A_{15}
 A_{15}
 A_{15}
 A_{15}
 A_{15}
 A_{15}
 A_{15}

wherein:

R₁₀ and R₁₄ are selected from the group consisting of hydroxy, oxo, amino, mercapto, alkylthio, alkyloxy, aryloxy, alkylamino, cycloalkylamino, aralkylamino, arylamino, diaralkylamino, diaralkylamino, diaralkylamino, and dialkylamino, where the alkyl groups are optionally linked to form a heterocycle; or

 R_{10} and R_{14} are acylamino according to Formula VI, provided that they incorporate an amino residue from the C-6 position of the purine or the C-4 position of the pyrimidine; or when R_{10} in a purine or R_{14} in a pyrimidine has as its first atom nitrogen, R_{10} and R_{11} or R_{14} and R_{15} are taken together to form a 5-membered fused imidazole ring, optionally substituted on the etheno ring with R_5 - R_9 selected from the group consisting of alkyl, cycloalkyl, aralkyl, or aryl moieties;

J is carbon or nitrogen, with the provision that when nitrogen, R_{12} is not present; R_{11} is hydrogen, \underline{O} or is absent;

 R_{12} is selected from the group consisting of hydrogen, alkyl, azido, alkylamino, arylamino, aralkylamino, alkoxy, aryloxy, aralkyloxy aralkoxy, alkylthio, arythio, aralkylthio, and ω -A(C₁. $_{6}$ alkyl)B- wherein A and B are selected from the group consisting of independently amino, mercapto, hydroxy and carboxyl;

R₁₃ is selected from the group consisting of hydrogen, chlorine, amino, monosubstituted amino, disubstituted amino, alkylthio, arylthio, and aralkylthio, where the substituent on sulfur contains up to a maximum of 20 carbon atoms, with or without unsaturation;

R₁₅ is selected from the group consisting of hydrogen, and acyl;

R₁₆ is selected from the group consisting of hydrogen, methyl, alkyl, halo, alkyl, alkenyl,

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substituted alkenyl, alkynyl, and substituted alkynyl;

Formula VI

wherein:

NH is the amino residue at the C-6 position in a purine or the amino residue at the C-4 position in a pyrimidine;

Q is a carbon atom;

W is oxygen or sulfur;

R₁₇ is amino or mono- or disubstituted amino such that the moiety according to formula VI is a urea or thiourea; or

R₁₇ is selected from the group consisting of alkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula VI is a carbamate or thiocarbamate; or

 R_{17} is selected from the group consisting of alkyl, cycloalkyl, aralkyl, and aryl, with or without substituents or heteroatoms, such that the moiety according to formula VI is an amide.

- 2. (Previously Presented) The compound according to Claim 38, wherein said compound is fluorescently labeled and used as a biochemical probe for the P2_T receptor.
- 3. (Previously Presented) A method of treating diseases or conditions associated with platelet aggregation comprising:

administering to a patient a pharmaceutical formulation according to Claim 1, wherein said compound is effective to bind the P2_T receptors on platelets and inhibit ADP-induced platelet aggregation.

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4. (Canceled).

5. (Previously Presented) The method according to Claim 3, wherein said pharmaceutical formulation is administered to reduce the incidence of dose-related adverse side effects of other therapeutic agents used to prevent, manage or treat platelet aggregation disorders.

- 6. (Previously Presented) The method according to Claim 3, wherein said administering is systemic administration of said compound.
- 7. (Original) The method according to Claim 6, wherein said systemic administration is administration of an injectable form of said compound, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.
- 8. (Previously Presented) The method according to Claim 6, wherein said systemic administration is accomplished by administering an oral form of said compound, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.
- 9. (Original) The method according to Claim 6, wherein said systemic administration is administration of said compound in a form of a transdermal patch or a transdermal pad, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.
- 10. (Original) The method according to Claim 6, wherein said systemic administration is administration of a liquid/liquid suspension of said compound via nose drops or nasal spray, or administration of a nebulized liquid to oral or nasopharyngeal airways of said subject, such that a therapeutically effective amount of said compound inhibits platelet aggregation.
- 11. (Previously Presented) The method according to Claim 6, wherein said systemic

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administration comprises infusion of said compound to target platelets via a device selected from the group consisting of a pump catheter system and a continuous or selective release device.

- 12. (Original) The method according to Claim 6, wherein said systemic administration is administration of a suppository form of said compound, such that a therapeutically effective amount of said compound contacts the target platelets of said patient via systemic absorption and circulation.
- 13. (Original) The method according to Claim 6, wherein said systemic administration is vaginal administration in dosage unit formulations containing conventional non-toxic pharmaceutically acceptable carriers, adjuvants and vehicles.
- 14. (Original) The method according to Claim 6, wherein said compound is administered to a patient by an intravitreal delivery.
- 15. (Original) The method according to Claim 6, wherein said systemic administration is administration of an intra-operative instillation of a gel, cream, powder, foam, crystals, liposomes, spray or liquid suspension form of said compound, such that a therapeutically effective amount of said compound contracts the target platelets of said patient via systemic absorption and circulation.
- 16. (Previously Presented) The method according to Claim 3, wherein said diseases or conditions associated with platelet aggregation are disorders or procedures characterized by thrombosis, primary arterial thrombotic complications of atherosclerotic disease, thrombotic complications of interventions of atherosclerotic disease, thrombotic complications of surgical or mechanical damage, mechanically induced platelet activation, shunt occlusion, thrombosis secondary to vascular damage and inflammation, indications with a diffuse thrombotic/platelet consumption component, venous thrombosis, coronary arterial thrombosis, pathological effects of atherosclerosis and arteriosclerosis, platelet aggregation and clot formation in blood and blood products during storage, chronic or acute states of hyper-aggregability, reocclusion of an artery or vein following fibrinolytic therapy, platelet adhesion associated with extracorporeal circulation, thrombotic complications associated with thrombolytic therapy, thrombotic complications

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associated with coronary and other angioplasty, or thrombotic complications associated with coronary artery bypass procedures.

- 17. (Previously Presented) The method according to Claim 16, wherein said disorders or procedures characterized with thrombosis are unstable angina, coronary angioplasty, or myocardial infarction.
- 18. (Previously Presented) The method according to Claim 16, wherein said primary arterial thrombotic complications of atherosclerosis are thrombotic stroke, peripheral vascular disease, or myocardial infarction without thrombolysis.
- 19. (Previously Presented) The method according to Claim 16, wherein said thrombotic complications of interventions of atherosclerotic disease are associated with angioplasty, endarterectomy, stent placement, coronary or other vascular graft surgery.
- 20. (Previously Presented) The method according to Claim 16, wherein said thrombotic complications of surgical or mechanical damage are associated with tissue salvage following surgical or accidental trauma, reconstructive surgery, or reductive surgery.
- 21. (Previously Presented) The method according to Claim 16, wherein said mechanically induced platelet activation is caused by cardiopulmonary bypass resulting in microthromboembolism.
- 22. (Previously Presented) The method according to Claim 16, wherein said shunt occlusion is renal dialysis or plasmapheresis.
- 23. (Previously Presented) The method according to Claim 16, wherein said thrombosis secondary to vascular damage and inflammation is vasculitis, arteritis, glomerulonephritis or

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organ graft rejection.

24. (Previously Presented) The method according to Claim 16, wherein said indications with

a diffuse thrombotic/platelet consumption component are disseminated intravascular coagulation,

thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, heparin-induced

thrombocytopenia, or pre-eclampsia/eclampsia.

25. (Previously Presented) The method according to Claim 16, wherein said venous

thrombosis is deep vein thrombosis, veno-occlusive disease, hematological conditions, or

migraine.

26. (Previously Presented) The method according to Claim 25, wherein said hematological

conditions are thrombocythemia or polycythemia.

27. (Previously Presented) The method according to Claim 16, wherein said coronary arterial

thrombosis is associated with unstable angina, coronary angioplasty or acute myocardial

infarction.

28. (Previously Presented) The method according to Claim 16, wherein pathological effects

of atherosclerosis and arteriosclerosis are arteriosclerosis, acute myocardial infarction, chronic

stable angina, unstable angina, transient ischemic attacks, strokes, peripheral vascular disease,

arterial thrombosis, preeclampsia, embolism, restenosis or abrupt closure following angioplasty,

carotid endarterectomy, or anastomosis of vascular grafts.

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29. (Previously Presented) The method according to Claim 16, wherein said chronic or acute states of hyper-aggregability is caused by DIC, septicemia, surgical or infectious shock, post-operative and post-partum trauma, cardiopulmonary bypass surgery, incompatible blood transfusion, abruptio placenta, thrombotic thrombocytopenic purpura, snake venom or immune

diseases.

- 30. (Original) The method according to Claim 16, wherein said reocclusion of an artery or vein following fibrinolytic therapy is inhibited by internal administration of said compound with a fibrinolytic agent.
- 31. (Previously Presented) The method according to Claim 30, wherein said fibrinolytic agent is selected from the group consisting of natural or synthetic products which directly or indirectly cause lysis of a fibrin clot.
- 32. (Previously Presented) The method according to Claim 30, wherein said fibrinolytic agent is a plasminogen activator selected from the group consisting of anistreplase, urokinase, pro-urokinase, streptokinase, tissue plasminogen activator and mutants or variants thereof, which retain plasminogen activator activity.
- 33. (Previously Presented) The method according to Claim 32, wherein said variants are selected from the group consisting of variants which have been chemically modified, variants which one or more amino acids have been added, deleted or substituted and variants with one or more modified functional domains.

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- 34. (Previously Presented) The method according to Claim 33, wherein said modified functional domains are added, deleted or altered by combining the active site of one plasminogen activator or fibrin binding domain with another plasminogen activator or fibrin binding molecule.
- 35. (Previously Presented) The pharmaceutical formulation according to Claim 1, wherein said formulation is sterile.
- 36. (Canceled)
- 37. (Previously Presented) The pharmaceutical formulation according to Claim 1, wherein said formulation further comprises a buffering agent.
- 38. (Currently Amended) A compound of general formula I, or salts thereof:

Formula I

$$A-O = \begin{bmatrix} T \\ P-X_3 \\ OM \end{bmatrix} \begin{bmatrix} W \\ P-X_2 \\ OM \end{bmatrix} \begin{bmatrix} V \\ P-X_1 \\ OM \end{bmatrix} \begin{bmatrix} T \\ N-P-Q \\ OM \end{bmatrix} OM \begin{bmatrix} N-P-Q \\ OM \end{bmatrix} \begin{bmatrix} N-P-Q \\$$

wherein:

 X_1 , X_2 , and X_3 are independently selected from the group consisting of oxygen, methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido; T, W, and V are independently oxygen or sulfur;

$$m = 0, 1 \text{ or } 2;$$

$$n=0, 1, or 2;$$

$$p=0, 1, or 2;$$

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M= H or a pharmaceutically-acceptable inorganic or organic counterion;

 $D_1 = O \text{ or } C$;

B' is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the 1' position of the furanose or carbocycle via the 9- or 1- position, respectively;

A is M or alkyl; or

A is a nucleoside residue which is defined as:

and which is linked to the phosphate chain via the 5' position of the furanose or carbocycle; wherein:

 $D_2 = O \text{ or } C$;

B is a purine or a pyrimidine residue according to general formulas IV and V which is linked to the sugar or carbocycle via the 9- or 1- position, respectively;

wherein when D_1 and D_2 are oxygen, the furanose is in the β -configuration;

Y'= H, OH, or OR₁, where OR₁ falls under the definition of general Formula II or III;

Z'= OH or OR₂, where OR₂ falls under the definition of general Formula II or III;

Z=OH or OR_3 , where OR_3 falls under the definition of general Formula II or III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general Formula II or III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively; wherein compounds of general Formula I are molecules whose structures fall within the definitions of Formula Ia and Formula Ib:

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Formula Ia

wherein:

 $X_1, X_2, \text{ and } X_3=0;$

T, V, and W = 0;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula II;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula II;

Z= OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively;

 $D_1 = 0;$

 $D_2 = O \text{ or } C$;

B and B' are purine or pyrimidine residues according to general formulas IV and V; m and p=0, 1 or 2;

n=0 or 1;

such that the sum of m+n+p is from 0 to 5; or

 $X_1, X_2, \text{ and } X_3=0;$

T, V, and W = O;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic eounterion; counterion;

 $D_1 = O$; Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula III;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III;

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provided that at least one of Y', Z', Z, and Y is OR1, OR2, OR3, or OR4, respectively;

 $D_2 = O$ or C;

B and B' are purine or pyrimidine residues according to general formulas IV and V;

m and p=0, 1 or 2;

n=0 or 1;

such that the sum of m+n+p is from 0 to 5; or

 X_1 and $X_3=0$;

X₂ is selected from the group consisting of methylene, monochloromethylene,

dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'= OH or OR₂, where OR₂ falls under the definition of general formula II;

Z=OH or OR₃, where OR₃ falls under the definition of general formula II;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula II;

provided that at least one of Y', Z', Z, and Y is OR1, OR2, OR3, or OR4, respectively;

 $D_1 = 0$;

 $D_2 = O \text{ or } C$;

B and B' are purine or pyrimidine residues according to general formulas IV and V;

m and p=0, 1 or 2;

n=1;

such that the sum of m+n+p is from [[0]] 1 to 5; or

 X_1 and $X_3=0$;

 X_2 is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M=H, NH_4^+ , Na^+ or other pharmaceutically-acceptable inorganic or organic counterion;

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Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula III; $Z' = OH \text{ or } OR_2$, where OR_2 falls under the definition of general formula III; Z= OH or OR₃, where OR₃ falls under the definition of general formula III; Y = H, OH, or OR₄, where OR₄ falls under the definition of general formula III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively; $D_1 = 0$; D_2 is O or C; B and B' are purine or pyrimidine residues according to general formulas IV and V; m and p = 0.1 or 2; n=1; such that the sum of m+n+p is from [[0]] 1 to 5; or X_1 and $X_3=0$; X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido; T=S: V and W=O; M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion; Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula II; Z'=OH or OR_2 , where OR_2 falls under the definition of general formula II; Z=OH or OR_3 , where OR_3 falls under the definition of general formula II; Y = H, OH, or OR₄, where OR₄ falls under the definition of general formula II; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively; $D_1 = 0;$ $D_2 = O \text{ or } C$; B and B' are purine or pyrimidine residues according to general formulas IV and V; m, n, and p=1; or X_1 and $X_3=0$; X₂ is selected from the group consisting of methylene, monochloromethylene,

dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

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T=S;

V and W=O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula III;

Z= OH or OR₃, where OR₃ falls under the definition of general formula III;

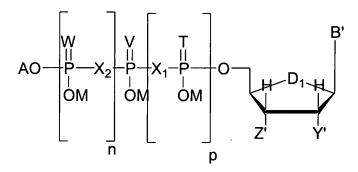
Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively;

 $D_1 = 0;$

 $D_2 = O \text{ or } C$;

B and B' are purine or pyrimidine residues according to general formulas IV and V; m, n, and p= 1;

Formula Ib



wherein:

A is M or alkyl;

 X_1 and $X_2 = O$;

T, V, and W = O;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula II;

Z'=H, OH or OR_2 , where OR_2 falls under the definition of general formula II;

with the provision that at least one of Y' and Z' is OR₁ or OR₂;

 $D_1 = O \text{ or } C$;

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n and p are 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or
A is M or alkyl;
X_1 and X_2 = O;
T, V, and W = O;
M is selected from the group consisting of H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> and other pharmaceutically-acceptable
inorganic or organic counterion;
Y' = OR_1, where R_1 falls under the definition of general formula III;
Z'=OR_2, where R_2 falls under the definition of general formula III;
D_1 = O \text{ or } C;
B' is purine or pyrimidine residue according to general formulas IV and V;
n and p are 0, 1, or 2 such that the sum of n+p is from [[1]] 0 to 3; or
A is M or alkyl;
X_1 and X_2 = O;
T and V = O;
W=S;
M= H, NH<sub>4</sub><sup>+</sup>, Na<sup>+</sup> or other pharmaceutically-acceptable inorganic or organic counterion;
Y'=H, OH, or OR<sub>1</sub>, where OR<sub>1</sub> falls under the definition of general formula II;
Z'=H, OH or OR<sub>2</sub>, where OR<sub>2</sub> falls under the definition of general formula II;
with the provision that at least one of Y' and Z' is OR<sub>1</sub> or OR<sub>2</sub>;
D_1 = O \text{ or } C;
B' is purine or pyrimidine residue according to general formulas IV and V;
p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;
n=1; or
A is M or alkyl;
X_1 and X_2 = O;
T and V = O;
W=S;
```

B' is purine or pyrimidine residue according to general formulas IV and V;

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M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

 $Y' = OR_1$, where OR_1 falls under the definition of general formula III;

 $Z' = OR_2$, where OR_2 falls under the definition of general formula III;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V;

p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;

n=1; or

A is M or alkyl;

 $X_1 = 0;$

 X_2 is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

Y'=H, OH, or OR₁, where OR₁ falls under the definition of general formula II;

Z'=H, OH or OR_2 , where OR_2 falls under the definition of general formula II; with the provision that at least one of Y' and Z' is OR_1 or OR_2 ;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V; p is 0, 1, or 2 such that the sum of n+p is from 1 to 3; n=1; or

A is M or alkyl;

 $X_1 = 0$;

X₂ is selected from the group consisting of methylene, monochloromethylene, dichloromethylene, monofluoromethylene, difluoromethylene, and imido;

T, V, and W = O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

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Y'= H, OH, or OR₁, where OR₁ falls under the definition of general formula III;

Z'=H, OH or OR₂, where OR₂ falls under the definition of general formula III;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V;

p is 0, 1, or 2 such that the sum of n+p is from 1 to 3;

n=1;

wherein, for compounds according to Formula Ia or Ib, where $Y' = OR_1$, $Z' = OR_2$, $Z = OR_3$ and/or $Y = OR_4$, at least one of the four is a residue which is linked directly to the corresponding 2' or 3' hydroxyl oxygen of the furanose or carbocycle via a carbon atom; wherein said residue falls within the scope of formula II or formula III:

Formula II

$$-0$$
 Q R_5 R_6

wherein:

O is the corresponding 2' or 3' oxygen of the furanose or carbocycle;

R₅, R₆, and R₇ are selected from the group consisting of H, an alkyl, cycloalkyl, aralkyl, aryl, and substituted aralkyl, and substituted aryl, such that the moiety defined according to formula II is an ether; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q, and R₇ is selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, and substituted aralkyl, and substituted aryl, such that the moiety defined according to formula II is an ester or thioester; or R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q, and R₇ is amino or mono- or disubstituted amino, where the substituents are selected from the group consisting of alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl, such that the moiety according to formula II is a carbamate or thiocarbamate; or

 R_5 and R_6 are taken together to be oxygen or sulfur doubly bonded to Q, and R_7 is selected from the group consisting of alkoxy, cycloalkoxy,

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aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula II is a carbonate or thiocarbonate; or

R₅ and R₆ are taken together to be oxygen or sulfur doubly bonded to Q and both the 2' and 3' oxygens of the furanose are directly bound to Q to form a cyclical carbonate or thiocarbonate, R₇ is not present;

Formula III

$$\leftarrow 0$$
 $\leftarrow 0$
 $\leftarrow R_{g}$

wherein:

O is the 2' and 3' oxygens of the furanose or carbocycle; and

the 2' and 3' oxygens of the furanose or carbocycle are linked by a common carbon atom to form a cyclical acetal, cyclical ketal, or cyclical orthoester; and

for cyclical acetals and ketals, R₈ and R₉ are independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl; or are joined together to form a homocyclic or heterocyclic ring composed of 3 to 8 atoms, or

for cyclical orthoesters, R_8 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, aralkyl, aryl, substituted aralkyl, and substituted aryl,

and R_9 is selected from the group consisting of alkyloxy, cycloalkyloxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy;

B and B' are independently a purine residue, as in formula IV, linked through the 9- position, or a pyrimidine residue, as in formula V, linked through the 1- position;

wherein, provided when D₁ and D₂ are oxygen, the ribosyl moieties are in the D- configuration;

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Formula V

$$\begin{array}{c|c} R_{14} \\ \hline \\ R_{16} \\ \hline \\ 5 \\ \hline \\ 6 \\ \hline \\ 2 \\ \hline \\ N \\ \hline \\ O \\ \\ \end{array}$$

wherein:

 R_{10} and R_{14} are selected from the group consisting of alkylthio, alkyloxy, aryloxy, cycloalkylamino, aralkylamino, arylamino, diaralkylamino, and diarylamino, and dialkylamino where the alkyl groups are optionally linked to form a heterocycle; or R_{10} and R_{14} are acylamino according to Formula VI, provided that they incorporate an amino residue from the C-6 position of the purine or the C-4 position of the pyrimidine; or when R_{10} in a purine or R_{14} in a pyrimidine has as its first atom nitrogen, R_{10} and R_{11} or R_{14} and R_{15} are taken together to form a 5-membered fused imidazole ring, optionally substituted on the etheno ring with R_{5} - R_{9} selected from the group consisting of alkyl, cycloalkyl, aralkyl, or aryl moieties;

J is carbon or nitrogen, with the provision that when nitrogen, R_{12} is not present;

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 R_{11} is hydrogen, \underline{O} or is absent;

R₁₂ is selected from the group consisting of hydrogen, alkyl, azido, alkylamino, arylamino, aralkylamino, alkoxy, aryloxy, aralkyloxy aralkoxy, alkylthio, arythio, aralkylthio, and ω-A(C₁-6alkyl)B- wherein A and B are selected from the group consisting of independently amino, mercapto, hydroxy and carboxyl;

R₁₃ is selected from the group consisting of hydrogen, chlorine, amino, monosubstituted amino, disubstituted amino, alkylthio, arylthio, and aralkylthio, where the substituent on sulfur contains up to a maximum of 20 carbon atoms, with or without unsaturation;

R₁₅ is selected from the group consisting of hydrogen, and acyl;

R₁₆ is selected from the group consisting of hydrogen, methyl, alkyl, halo, alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl;

Formula VI

$$-\overset{H}{\overset{W}{\overset{}}}$$

wherein:

NH is the amino residue at the C-6 position in a purine or the amino residue at the C-4 position in a pyrimidine;

Q is a carbon atom;

W is oxygen or sulfur;

R₁₇ is amino or mono- or disubstituted amino such that the moiety according to formula VI is a urea or thiourea; or

 R_{17} is selected from the group consisting of alkoxy, aralkyloxy, aryloxy, substituted aralkyloxy, and substituted aryloxy, such that the moiety according to formula VI is a carbamate or thiocarbamate; or

R₁₇ is selected from the group consisting of alkyl, cycloalkyl, aralkyl, and aryl, with or without substituents or heteroatoms, such that the moiety according to formula VI is an amide.

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39. (Previous Presented) The pharmaceutical formulation of Claim 1 wherein said compound is a compound of Formula I:

Formula I

wherein:

V = 0;

n = m = p = 0;

A=M;

M = H or a pharmaceutically-acceptable inorganic or organic counterion;

 $D_1 = 0$;

Formula III

$$\leftarrow 0$$
 R_9

wherein:

O is the 2' and 3' oxygens of the furanose; and

the 2' and 3' oxygens of the furanose are linked by a common carbon atom to form a cyclical acetal; and

R₈ is hydrogen; and

R₉ is selected from the group consisting of aralkyl, aryl, substituted aralkyl, and substituted aryl; in which the aralkyl groups are from 1 to 5 carbons in the alkyl portion, and are: monocyclic

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moieties from 4 to 8 carbons without heteroatoms in the aryl portion; and the aryl groups are monocyclic moieties from 4 to 8 carbons, without heteroatoms;

B' is a purine residue according to general Formula IV wherein:

R₁₀ is acylamino, according to Formula VI;

W is oxygen; and

R₁₇ is amino or mono- or disubstituted amino such that the moiety according to Formula VI is a urea;

J = carbon;

 R_{11} is absent;

R₁₂ is hydrogen; and

R₁₃ is hydrogen.

40. (New) The pharmaceutical formulation according to Claim 1, wherein said compound is Formula Ia, wherein

 $X_1, X_2, \text{ and } X_3=0;$

T, \overrightarrow{V} , and W= O;

M= H, NH₄⁺, Na⁺ or other pharmaceutically-acceptable inorganic or organic counterion;

Y'= H, OH, or OR_1 , where OR_1 falls under the definition of general formula III;

Z'=OH or OR_2 , where OR_2 falls under the definition of general formula III;

Z=OH or OR₃, where OR₃ falls under the definition of general formula III;

Y= H, OH, or OR₄, where OR₄ falls under the definition of general formula III; provided that at least one of Y', Z', Z, and Y is OR₁, OR₂, OR₃, or OR₄, respectively;

 $D_1 = 0;$

 $D_2 = 0;$

B and B' are purine or pyrimidine residues according to general formulas IV and V;

m and p=0, 1 or 2;

n=0 or 1.

such that the sum of m+n+p is from 0 to 5.

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41. (New) The pharmaceutical formulation according to Claim 1, wherein said compound is Formula Ib, wherein

A is M or alkyl;

 X_1 and $X_2 = O$;

T, V, and W = O;

M is selected from the group consisting of H, NH₄⁺, Na⁺ and other pharmaceutically-acceptable inorganic or organic counterion;

 $Y' = OR_1$, where OR_1 falls under the definition of general formula III;

 $Z' = OR_2$, where OR_2 falls under the definition of general formula III;

 $D_1 = O \text{ or } C$;

B' is purine or pyrimidine residue according to general formulas IV and V; n and p are 0, 1, or 2 such that the sum of n+p is from 0 to 3.

42. (New) The pharmaceutical formulation according to Claim 1, wherein R₁₀ and R₁₄ are selected from the group consisting of aryloxy, cycloalkylamino, aralkylamino; and acylamino according to Formula VI;

J is carbon;

 R_{11} is absent;

R₁₂ is hydrogen, alkyl, alkylamino, aralkylamino, aralkoxy, or aralkylthio;

R₁₃ is hydrogen, chlorine, disubstituted amino, alkylthio, or aralkylthio;

R₁₅ is hydrogen; and

 R_{16} is hydrogen, halo, or alkyl.

- 43. (New) The method according to Claim 3, wherein said pharmaceutical formulation is a pharmaceutical formulation according to Claim 39.
- 44. (New) The method according to Claim 3, wherein said pharmaceutical formulation is a pharmaceutical formulation according to Claim 40.
- 45. (New) The method according to Claim 3, wherein said pharmaceutical formulation is a pharmaceutical formulation according to Claim 41.

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46. (New) The method according to Claim 3, wherein said pharmaceutical formulation is a pharmaceutical formulation according to Claim 42.